World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2025 August 28; 31(32): 108827

DOI: 10.3748/wjg.v31.i32.108827

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

MINIREVIEWS

Interplay between endocrine disorders and liver dysfunction: Mechanisms of damage and therapeutic approaches

Andres M Vargas-Beltran, Samantha M Armendariz-Pineda, Froylan D Martínez-Sánchez, Carolina Martinez-Perez, Aldo Torre, Jacqueline Cordova-Gallardo

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade B, Grade B

Novelty: Grade B, Grade B, Grade B

Creativity or Innovation: Grade B, Grade B, Grade C

Scientific Significance: Grade B, Grade B, Grade B

P-Reviewer: He YH, MD, Associate Chief Physician, China; Sun JZ, Professor, China

Received: April 27, 2025

Revised: June 3, 2025

Accepted: August 1, 2025

Published online: August 28, 2025

Processing time: 123 Days and 4.8 Hours

Andres M Vargas-Beltran, Samantha M Armendariz-Pineda, Carolina Martinez-Perez, Jacqueline Cordova-Gallardo, Department of Hepatology, General Hospital Dr. Manuel Gea Gonzalez, Mexico City 14080, Mexico

Andres M Vargas-Beltran, Faculty of Medicine, Meritorious Autonomous University of Puebla, Puebla 72420, Mexico

Samantha M Armendariz-Pineda, Froylan D Martínez-Sánchez, Jacqueline Cordova-Gallardo, Faculty of Medicine, National University Autonomous of Mexico, Mexico City 04360, Mexico

Froylan D Martínez-Sánchez, Department of Internal Medicine, General Hospital Dr. Manuel Gea Gonzalez, Mexico City 14080, Mexico

Aldo Torre, Department of Gastroenterology, Centro Médico ABC, Mexico City 05300, Mexico

Co-corresponding authors: Aldo Torre and Jacqueline Cordova-Gallardo.

Corresponding author: Jacqueline Cordova-Gallardo, MD, Doctor, Faculty of Medicine, National University Autonomous of Mexico, Escolar 411A, Copilco Universidad, Coyoacán, Mexico City 04360, Mexico. jacqueline.cordova@comunidad.unam.mx

Abstract

Endocrine disorders frequently lead to metabolic disturbances that significantly affect liver function. Understanding the complex interplay between hormonal imbalances and liver dysfunction is essential for advancing targeted therapeutic strategies. This comprehensive review explores the pathophysiological mechanisms linking major endocrine disorders to liver disease, with a focus on the roles of the thyroid, parathyroid, pancreas, adrenal glands, and sex hormones. Thyroid dysfunction is associated with alterations in liver enzyme levels and metabolic regulation, often resulting in hepatic steatosis or cholestasis. Hyperparathyroidism and consequent hypercalcemia have been linked to hepatic calcifications. Insulin resistance, both hepatic and peripheral, contributes to excessive lipid accumulation in the liver, exacerbating steatotic changes. Adrenal gland disorders, particularly in the setting of chronic liver disease, impair cortisol metabolism and may worsen hepatic injury. Additionally, sex hormones such as estrogen and testosterone modulate the progression of liver fibrosis and influence the development of metabolic syndrome. The intricate relationship between endocrine and hepatic systems underscores the need for a multidisciplinary approach in the ma-

nagement of liver disease. Addressing underlying hormonal disturbances may enhance patient outcomes and prevent further hepatic deterioration. Future research should prioritize integrative therapeutic strategies that concurrently target endocrine and liver dysfunction.

Key Words: Liver disease; Hormonal imbalance; Endocrine disorders; Cirrhosis; Liver dysfunction; Liver pathology; Metabolic liver disease

©The Author(s) 2025. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: This review highlights the intricate relationship between endocrine disorders and liver dysfunction, emphasizing the role of hormonal imbalances in the development and progression of liver disease. By examining the effects of thyroid, parathyroid, pancreatic, adrenal, and sex hormones on hepatic metabolism and injury, the article provides a comprehensive overview of pathophysiological mechanisms and emerging therapeutic strategies. Understanding these endocrine-hepatic interactions is essential for early recognition, improved patient management, and the development of targeted treatments in metabolic and chronic liver diseases.

Citation: Vargas-Beltran AM, Armendariz-Pineda SM, Martínez-Sánchez FD, Martinez-Perez C, Torre A, Cordova-Gallardo J. Interplay between endocrine disorders and liver dysfunction: Mechanisms of damage and therapeutic approaches. *World J Gastroenterol* 2025; 31(32): 108827
URL: https://www.wjgnet.com/1007-9327/full/v31/i32/108827.htm
DOI: https://dx.doi.org/10.3748/wjg.v31.i32.108827

INTRODUCTION

The liver is a vital organ responsible for numerous essential functions, including detoxification, nutrient metabolism, bile production, and glucose regulation. Systemic diseases, including endocrine disorders, can impair liver function, leading to hepatic inflammation, enzyme abnormalities, and various structural changes such as steatosis, hypoxic injury, or calcification. Hormonal imbalances in conditions such as diabetes mellitus, thyroid dysfunction, adrenal insufficiency, and hypogonadism often contribute to these hepatic alterations (Figure 1).

Conversely, chronic liver diseases, particularly, advanced chronic liver disease (ACLD). and metabolic dysfunction-associated steatotic liver disease (MASLD), disrupt endocrine homeostasis. Liver dysfunction impairs hormone metabolism and clearance, alters the hypothalamic-pituitary axis, and induces systemic inflammation. These processes result in clinical manifestations such as insulin resistance, gonadal dysfunction, thyroid abnormalities, and adrenal insufficiency[1-3].

This review explores the complex bidirectional relationship between the endocrine system and the liver. We examine how endocrine disorders affect hepatic physiology and how liver disease alters hormonal pathways. Specific emphasis is given to pathophysiological mechanisms, clinical implications, and therapeutic considerations, aiming to guide multidisciplinary care and highlight emerging areas for research[4,5].

INTERACTION BETWEEN ENDOCRINE ORGANS AND HEPATIC FUNCTION

The role of the thyroid gland

The liver plays a central role in metabolizing thyroid hormones, thyroxine (T4) and triiodothyronine (T3), which regulate hepatocyte metabolism, growth, and development through nuclear and mitochondrial receptors. These hormones influence carbohydrate, lipid, and protein metabolism by modulating glucose transporter expression, glycogen synthesis, β-oxidation, lipoprotein lipase activity, and protein turnover. Consequently, thyroid dysfunction can significantly alter liver function tests due to disruptions in these metabolic pathways (Figure 2)[5,6].

Hypothyroidism impairs lipid clearance by reducing hepatic lipase activity, contributing to triglyceride accumulation and hepatic steatosis. It may also disrupt adipocytokines such as leptin, adiponectin, and tumor necrosis factor (TNF)-α, promoting hepatic inflammation and fibrosis. A prospective cohort study reported an increased risk of MASLD in individuals with hypothyroidism compared to euthyroid subjects[5].

Reduced uridine diphosphate-glucuronosyltransferase activity decreases bilirubin conjugation, leading to intrahepatic cholestasis and unconjugated hyperbilirubinemia. Additionally, hypothyroidism downregulates canalicular transporters like multidrug resistance-associated protein 2, further impairing bile excretion[7]. Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels may result from cholestasis or hypothyroid-induced myopathy. A study of 60 hypothyroid and 40 euthyroid women found significantly higher transaminase levels in the hypothyroid group, with thyroid stimulating hormone (TSH) positively correlating with enzyme elevation[6,8].

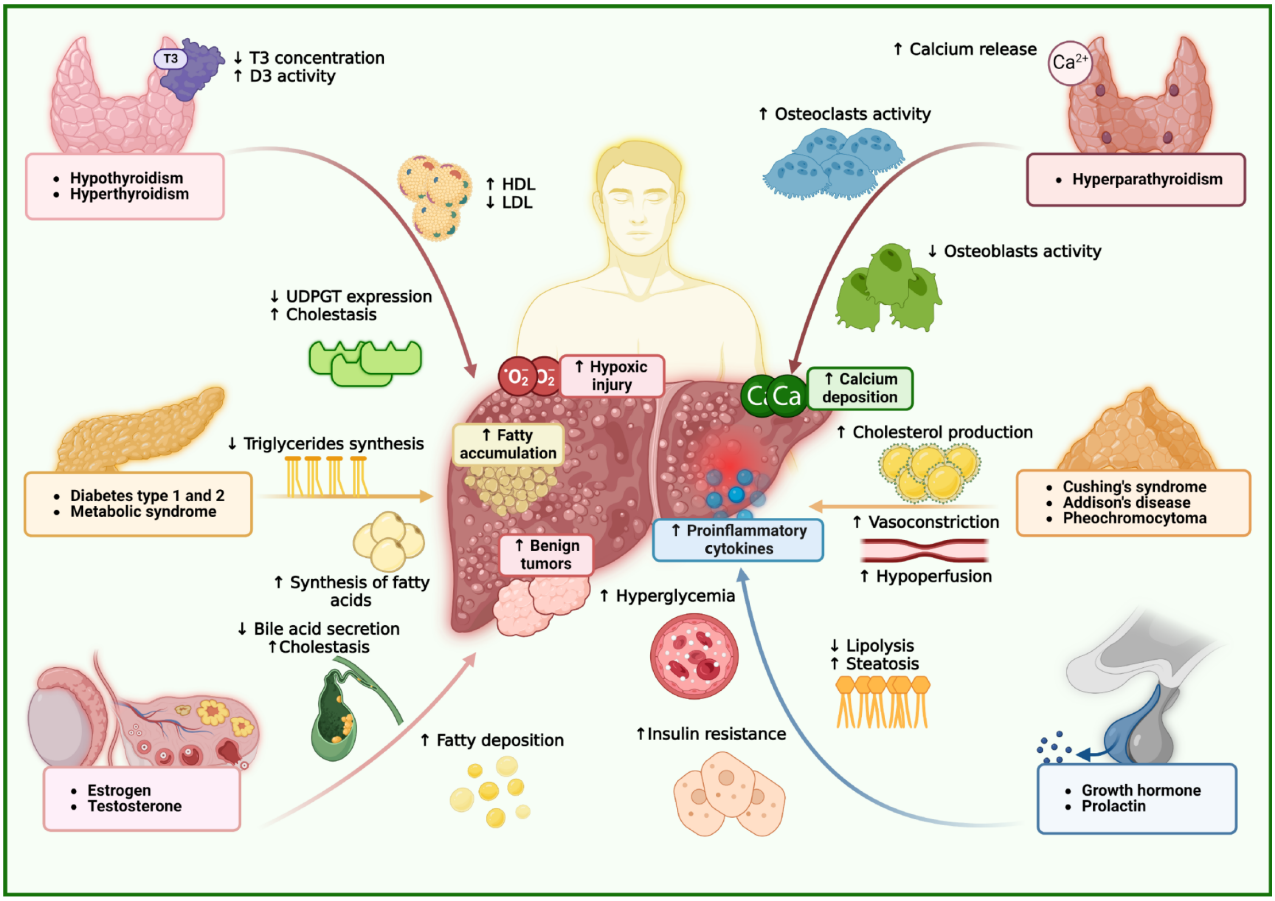

Figure 1 Interactions between endocrine organs and hepatic function. In hypothyroidism, reduced triiodothyronine levels impair β-oxidation and downregulate uridine diphosphate-glucuronosyltransferase, leading to lipid accumulation and defective bilirubin conjugation, which contribute to cholestasis. Elevated tumor necrosis factor-α and decreased deiodinase activity further exacerbate liver dysfunction. In contrast, hyperthyroidism increases metabolic rate and hepatic oxygen demand, accelerating lipid turnover but inducing hepatocellular injury through oxidative stress and hypoxia. This results in reduced low-density lipoprotein levels and paradoxically elevated high-density lipoprotein, possibly due to increased apolipoprotein A1 synthesis. In adrenal dysfunction, hyperaldosteronism activates mineralocorticoid receptor and epithelial sodium channel, causing sodium retention, ascites, and edema compounded by oxidative stress. Hypercortisolism enhances gluconeogenesis and hepatic lipid accumulation, raising the risk of metabolic dysfunction-associated steatotic liver disease, while adrenal insufficiency impairs anti-inflammatory responses, promoting inflammation. Sex hormones also modulate hepatic physiology. Low testosterone decreases glucose transporter type 4 activity, contributing to insulin resistance and sarcopenia. Increased aromatase activity converts testosterone to estradiol, leading to hyperestrogenism, cholestasis, and benign hepatic tumors. Estrogen signaling through estrogen receptor α offers protective effects by reducing oxidative stress and inflammation, thereby mitigating steatosis and fibrosis. In contrast, growth hormone and prolactin have been associated with increased hepatic steatosis. D3: Type 3 deiodinase; Ca: Calcium; O_2: Oxygen; T3: Triiodothyronine; UDPGT: Uridine diphosphate-glucuronosyltransferase; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

Thyroid dysfunction may also impair bile flow *via* reduced sphincter of Oddi relaxation, increasing the risk of biliary stones. These can develop before or persist despite treatment, underscoring the importance of therapeutic monitoring. Clinical overlap between hypothyroidism and ACLD can lead to diagnostic challenges. For instance, ascites in myxedema, due to increased endothelial permeability, is typically protein-rich and resolves with thyroid hormone replacement[9,10].

Recent advances in managing thyroid-associated MASLD emphasize both conventional and emerging treatments. In overt hypothyroidism, especially with concurrent dyslipidemia, levothyroxine therapy has been shown to improve hepatic lipid metabolism and reduce MASLD severity. Even in subclinical hypothyroidism, restoring euthyroid status may help slow liver disease progression[11,12]. The development of thyroid hormone receptor β (THRβ)-selective agonists offers a targeted approach to treating metabolic liver diseases. Resmetirom, a potent and selective THRβ agonist, reduces hepatic fat content and inflammation while avoiding systemic thyrotoxic effects such as cardiotoxicity. It recently gained Food and Drug Administration approval for treating non-alcoholic steatohepatitis (NASH) with moderate to advanced fibrosis, based on clinical trials demonstrating significant histological and biochemical improvements. Several other THRβ agonists are currently in various stages of clinical development.

Additionally, emerging therapies include thyroid hormone analogs like 3,5-diiodo-L-thyronine and liver-specific prodrugs designed to enhance hepatic effects while minimizing systemic exposure. While these agents have shown favorable outcomes in preclinical studies, further research is needed to confirm their safety and efficacy in humans[13]. In contrast, hyperthyroidism can cause hepatic damage in either a hepatocellular or cholestatic pattern due to increased oxygen demand across multiple organs, including the liver. Hyperthyroidism can lead to liver dysfunction through multiple interrelated mechanisms. Excess thyroid hormones increase hepatic oxygen demand and metabolic activity, which may outpace blood supply, particularly in perivenular regions, resulting in hypoxic injury. This imbalance also

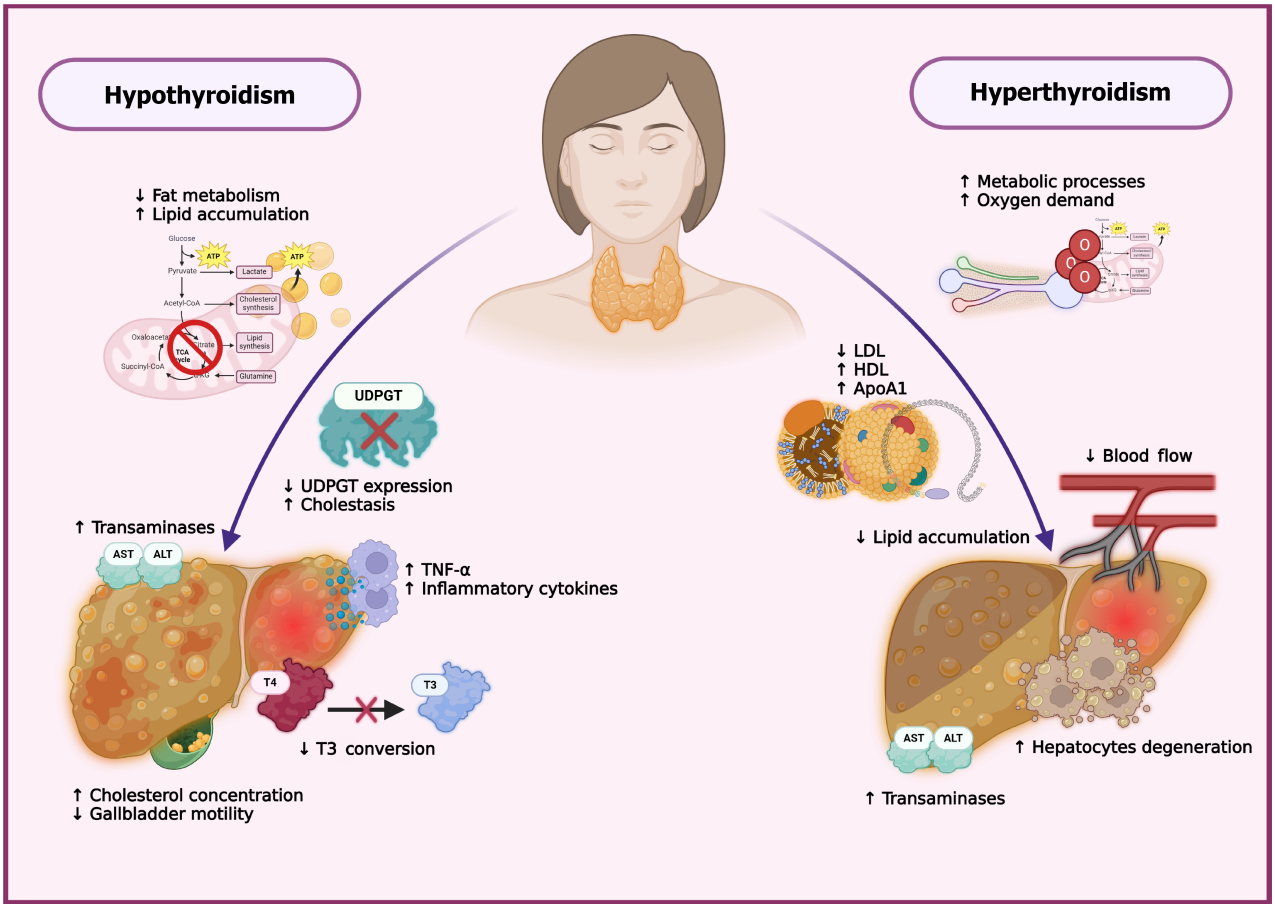

Figure 2 The role of the thyroid gland. In hypothyroidism, reduced levels of thyroxine (T4) and triiodothyronine (T3) lower the basal metabolic rate and impair lipid metabolism, leading to hepatic lipid accumulation due to decreased β-oxidation and suppressed lipolytic gene expression. It also reduces uridine diphosphate-glucuronosyltransferase activity, impairing bilirubin conjugation and promoting cholestasis. Diminished D1 activity limits T4-to-T3 conversion, and elevated proinflammatory cytokines like tumor necrosis factor-α contribute to hepatocellular injury and increased transaminase levels. Hypothyroidism also impairs low-density lipoprotein (LDL) clearance and bile acid synthesis, raising serum cholesterol and reducing gallbladder motility. Conversely, hyperthyroidism accelerates lipid metabolism and stimulates lipoprotein lipase activity, which decreases LDL levels. Despite this, high-density lipoprotein concentrations tend to rise, possibly due to enhanced synthesis of apolipoprotein A1. However, increased oxidative stress and hepatic oxygen demand can lead to hepatocyte damage, particularly in centrilobular zones. These contrasting effects emphasize the bidirectional relationship between thyroid status and liver health. ATP: Adenosine triphosphate; TCA: Tricarboxylic acid cycle; T3: Triiodothyronine; UDPGT: Uridine diphosphate-glucuronosyltransferase; T4: Thyroxine; TNF: Tumor necrosis factor; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ApoA1: Apolipoprotein A1; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

promotes oxidative stress through elevated production of reactive oxygen species, contributing to hepatocellular damage. Experimental and clinical studies have shown increased lipid peroxidation, glutathione depletion, and histological signs of inflammation and necrosis in such cases. While liver injury is often transient, severe cases, including acute hepatic failure, have been reported. This can lead to hypoxic injury in the perivenular regions resulting from inadequate perfusion of hepatocytes. Although this hepatic injury is usually self-limited, cases of acute hepatic failure associated with hyperthyroidism have been reported[14-16].

Cholestatic damage, characterized by elevated levels of alkaline phosphatase, gamma-glutamyl transferase, and bilirubin, can occur in patients with thyrotoxicosis, particularly those with heart failure or sepsis[14,17]. Although the exact mechanisms remain unclear, hyperthyroidism may affect liver function through direct alterations in hepatocyte metabolism, increased hepatic oxygen demand, and relative hypoxia, particularly in centrilobular zones. In some cases, thyrotoxicosis-related cardiac dysfunction may further impair hepatic perfusion. However, cholestatic liver injury has also been observed in the absence of cardiac or infectious causes. Notably, case reports and series have described severe cholestatic jaundice as an initial manifestation of hyperthyroidism, which often resolves with antithyroid therapy or radioiodine (I-131) ablation following restoration of euthyroidism[18,19].

Another potential cause of liver injury in hyperthyroid patients is drug-induced liver injury (DILI) from antithyroid medications, typically occurring within the first 2-3 months of therapy initiation[20]. Propylthiouracil carries a higher risk of hepatotoxicity compared to methimazole (MMI), primarily due to oxidative stress, as demonstrated by *in vitro* studies using the DILI system model. Routine liver function testing during the initial months of treatment is recommended to detect early signs of toxicity[21-23].

Managing hyperthyroidism in patients with underlying liver dysfunction is particularly challenging. Thionamides, including MMI and carbimazole, can cause liver injury most often cholestatic, but hepatocellular damage is also reported. If hepatotoxicity is suspected, these agents should be discontinued in favor of alternative therapies. I-131 offers a safer

option, especially in those with preexisting hepatic impairment, and has been associated with improvements in both thyroid and liver function markers. In severe cases, artificial liver support systems such as the molecular adsorbent recirculating system may help stabilize hepatic function, allowing safer use of I-131[24,25].

Parathyroid glands, bone health, and liver problems

Although not fully understood, the liver-parathyroid axis primarily involves the regulation of calcium and phosphate metabolism, which is often disrupted in chronic liver disease. Parathyroid hormone (PTH), essential for calcium homeostasis, may be dysregulated in liver dysfunction, contributing to secondary hyperparathyroidism and hepatic osteodystrophy[26,27].

In cirrhosis, reduced hepatic production of insulin-like growth factor-1 (IGF-1) is associated with impaired bone mineralization and increased osteoporosis risk. Lower IGF-1 Levels correlate with liver dysfunction, fibrogenesis, and mortality in ACLD, primarily through disrupted bone remodeling, marked by reduced osteoblast activity and prolonged osteoclast lifespan[28,29].

Growing interest surrounds the osteoprotegerin (OPG)/receptor activator for nuclear factor-κB ligand (RANKL)/receptor activator of nuclear factor-kappa B axis, which links bone metabolism to liver pathology. Dysregulation of this system has been implicated in MASLD and type 2 diabetes. Although elevated OPG may initially protect bone, it can contribute to hepatic steatosis and fibrogenesis, exacerbating liver damage[26,30].

High PTH levels have also been associated with MASLD and may serve as a biomarker for disease presence. Although a direct link with metabolic dysfunction-associated steatohepatitis (MASH) was not statistically significant, the data suggest a potential pathogenic role[26]. Moreover, hypercalcemia due to primary hyperparathyroidism can lead to hepatic calcifications and gallstones, further compromising liver function. These findings underscore the importance of monitoring PTH, calcium, IGF-1, and OPG/RANKL in patients with chronic liver disease to preserve bone health and prevent hepatic complications[31].

The pancreas-liver axis: Hormonal interactions in glucose and lipid metabolism

The pancreas and liver are interconnected *via* the pancreas-liver axis, regulating glucose and lipid metabolism. The pancreas produces insulin from β-cells and glucagon from α-cells, which have opposing effects on hepatic metabolism. Insulin promotes glucose uptake, glycogen synthesis, and lipogenesis, while glucagon stimulates glycogenolysis, gluconeogenesis, and fatty acid β-oxidation[1,32,33].

Hepatic *vs* peripheral insulin resistance: Hepatic insulin resistance occurs when the liver becomes less responsive to insulin, resulting in increased gluconeogenesis and glycogenolysis. This impairment is commonly driven by obesity, chronic inflammation, and the accumulation of free fatty acids[34-36]. At the molecular level, insulin signaling in hepatocytes primarily involves the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt) pathway, which promotes glucose uptake, glycogen synthesis, and lipid regulation. Akt activation leads to phosphorylation of key targets such as *GSK3β*, enhancing glycogen synthase activity, and *FOXO1*, suppressing gluconeogenic enzymes[26-28,30]. Dysfunction in PI3K or Akt impairs these processes, and alternate pathways like *Raf1*/extracellular regulated protein kinases/mitogen-activated protein kinase may become involved, although less effectively[32,34].

In contrast, peripheral insulin resistance affects skeletal muscle, adipose tissue, and other organs, leading to reduced glucose uptake and utilization. Unlike hepatic insulin resistance, which primarily alters glucose production, peripheral resistance limits systemic glucose disposal, contributing to hyperglycemia, particularly in type 2 diabetes[32,34,36]. Obesity, sedentary lifestyle, and chronic inflammation, mediated by reactive metabolites, cytokines, and adipokines, are key contributors to this resistance. These factors disrupt insulin receptor signaling and downstream effectors across multiple organs, including muscle, heart, kidney, and pancreas. Age-related reductions in muscle mass and vascular changes further exacerbate insulin resistance[36-38].

Lifestyle modification remains the cornerstone of treatment. Weight loss through diet and exercise improves insulin sensitivity and liver histology in MASLD/NASH. Among pharmacologic options, pioglitazone shows the strongest evidence for improving steatosis and inflammation, and potentially fibrosis, though its use is limited by side effects and contraindications in decompensated cirrhosis. glucagon-like peptide-1 receptor agonists promote weight loss and NASH resolution, with semaglutide showing significant efficacy in improving histology without worsening fibrosis. Sodium-dependent glucose transporters 2 inhibitors may also reduce hepatic fat and improve metabolic parameters, although histological benefits remain uncertain. Meanwhile, metformin and dipeptidyl peptidase 4 inhibitors have not demonstrated consistent histological improvements, although metformin may confer some protection against hepatocellular carcinoma in observational studies[39,40].

Hyperglucagonemia and hepatic lipid accumulation: Hyperglucagonemia, commonly observed in type 2 diabetes, plays a significant role in hepatic lipid dysregulation and the progression of MASLD. Elevated glucagon activates the cyclic adenosine monophosphate/protein kinase A signaling pathway in hepatocytes, leading to phosphorylation of enzymes such as hormone-sensitive lipase and acetyl-CoA carboxylase (ACC). Inhibition of ACC decreases malonyl-CoA levels, relieving suppression of carnitine palmitoyl transferase 1 and enhancing fatty acid transport into mitochondria for β-oxidation[32,41,42].

However, chronic glucagon elevation drives persistent gluconeogenesis and amino acid catabolism, increasing substrates like glycerol, acetyl-CoA, and free fatty acids. These excess substrates are diverted toward *de novo* lipogenesis, contributing to hepatic triglyceride accumulation. Glucagon also suppresses follistatin, impairing lipid metabolism regulation and promoting steatosis. Moreover, glucagon signaling influences key genes such as *PNPLA3*, associated with impaired triglyceride hydrolysis and MASLD susceptibility[34,36,41].

Additionally, hyperglucagonemia alters mitochondrial function by modulating energy-sensing factors like peroxisome proliferator-activated receptor-gamma coactivator-1α, promoting lipid accumulation and hepatic inflammation. This imbalance between lipid oxidation and synthesis fosters lipotoxicity, driving the progression from MASLD to MASH[41,42].

Chronic low-grade inflammation and interleukin-1: Chronic low-grade inflammation, particularly involving interleukin (IL)-1, is a key factor in developing insulin resistance and liver dysfunction[34,36]. IL-1 plays a pivotal role in the development of insulin resistance and liver dysfunction, particularly in the setting of obesity, Metabolic syndrome, type 2 diabetes, and MASH. This condition is marked by sustained activation of innate immune pathways in metabolic organs such as adipose tissue and the liver, triggered by excess nutrients and adipocyte hypertrophy.

In hypertrophic adipose tissue, enlarged fat cells release higher levels of proinflammatory cytokines, including IL-1. These signals drive the infiltration and activation of macrophages toward a classically activated proinflammatory phenotype. Together with other innate immune cells, they amplify local and systemic inflammation. This inflammatory environment disrupts insulin signaling through activation of kinases such as c-Jun N-terminal kinase and IκB kinase β, which promote serine phosphorylation of insulin receptor substrates, thereby impairing insulin signal transduction and glucose uptake. Additionally, inflammation enhances lipolysis within adipose tissue, leading to elevated levels of circulating free fatty acids. These free fatty acids accumulate in the liver and skeletal muscle, contributing to ectopic fat deposition, lipotoxicity, and further insulin resistance[43-45]. In the liver, IL-1-driven inflammation contributes to hepatic steatosis, fibrosis, and the progression to MASH[33,34]. Furthermore, IL-1 can disrupt β-cell function in the pancreas, reducing insulin secretion and perpetuating hyperglycemia[46]. In MASH, dysregulated secretion of hepatokines plays a crucial role in the pathophysiology of MASLD and its progression to steatohepatitis and fibrosis. Fetuin-A is a key hepatokine upregulated by free fatty acids and glucose; it promotes insulin resistance by inhibiting insulin receptor activity in the liver and muscle and activates toll-like receptor 4, inducing inflammation[47]. High fetuin-A levels correlate with insulin resistance and increased liver fat, especially with elevated free fatty acids. Dysregulated hepatokines in MASLD, like angiopoietin-like protein 3, inhibit lipoprotein lipase, causing dyslipidemia and insulin resistance. Similarly, fibroblast growth factor 21, often elevated in MASLD, regulates glucose and lipid metabolism as a stress hormone. However, its efficacy is blunted in the context of hepatic insulin resistance. Dysregulated hepatokines reveal the complex link between liver function, metabolism, and inflammation, suggesting potential therapeutic targets in MASLD[34,36,42].

In the setting of MASLD, IL-1-driven inflammation not only contributes to hepatic steatosis and fibrosis but also modulates the secretion of key hepatokines that influence systemic metabolism. For example, while fetuin-A is typically upregulated by free fatty acids and glucose, promoting insulin resistance through inhibition of insulin receptor activity and activation of toll-like receptor 4, its expression is downregulated during acute IL-1-mediated inflammation *via* transcriptional repression mechanisms. Specifically, IL-1 alters CCAAT/enhancer binding protein isoform binding at the fetuin-A promoter, decreasing transcription and secretion of fetuin-A, consistent with its role as a negative acute-phase protein[48]. Nonetheless, in chronic metabolic conditions such as MASLD, persistently high free fatty acid levels may override this regulatory mechanism, leading to elevated circulating fetuin-A. Other hepatokines also contribute to the metabolic dysfunction seen in MASLD: Angiopoietin-like protein 3 inhibits lipoprotein lipase activity, promoting dyslipidemia and insulin resistance, while fibroblast growth factor 21, though elevated in MASLD, shows reduced efficacy due to hepatic insulin resistance. Together, these interactions illustrate how IL-1 and hepatokine dysregulation intersect the progression of MASLD, highlighting potential targets for therapeutic intervention[47].

The crosstalk between the adrenal glands and liver

Cortisol: Various metabolic and hormonal pathways link the adrenal glands and the liver, making adrenal hormones such as cortisol and aldosterone critical in regulating metabolism and maintaining liver function (Figure 3)[4,49]. Cortisol, produced by the adrenal glands, plays a vital role in stress response and glucose regulation by stimulating gluconeogenesis in the liver, thus ensuring glucose availability during periods of fasting or stress[49,50].

Nevertheless, chronic elevations in cortisol, as seen in Cushing's syndrome, can result in hyperglycemia and insulin resistance, which are significant contributors to MASLD[50]. Rockall *et al*[51] found that high cortisol levels promote liver fat accumulation and increased cholesterol synthesis, raising the risk of metabolic diseases. Their study reported hepatic steatosis in only 20% of Cushing's syndrome patients, with progression ranging from simple steatosis to cirrhosis.

Conversely, patients with Addison's disease, characterized by insufficient cortisol production, often suffer from hypoglycemia, which can impair liver function. The lack of cortisol can lead to metabolic stress and trigger the release of pro-inflammatory cytokines, further disrupting liver function[52,53]. In ACLD, systemic inflammation and stress trigger a compensatory increase in cortisol production. The liver plays a key role in cortisol metabolism through inactivation by 5α- and 5β-reductases and regeneration by 11β-hydroxysteroid dehydrogenase type 1 (HSD1). In chronic liver disease, this metabolic capacity is impaired, leading to reduced cortisol clearance and a relative increase in free cortisol levels, even when total levels appear normal or low. This shift is partly due to decreased corticosteroid-binding globulin and diminished hepatic breakdown, which may heighten sensitivity to corticosteroids and contribute to features resembling hypercortisolism, including hypertension, hyperglycemia, and muscle wasting[54].

Aldosterone: Aldosterone, a mineralocorticoid hormone produced by the adrenal glands, plays a pivotal role in fluid retention, electrolyte balance, and the progression of liver diseases such as cirrhosis. In liver dysfunction, secondary hyperaldosteronism develops because of reduced effective arterial blood volume due to splanchnic vasodilation and portal hypertension (Figure 4)[55]. This condition activates the renin-angiotensin-aldosterone system (RAAS), producing excessive aldosterone secretion, which promotes sodium retention, ascites and worsened portal hypertension. An animal

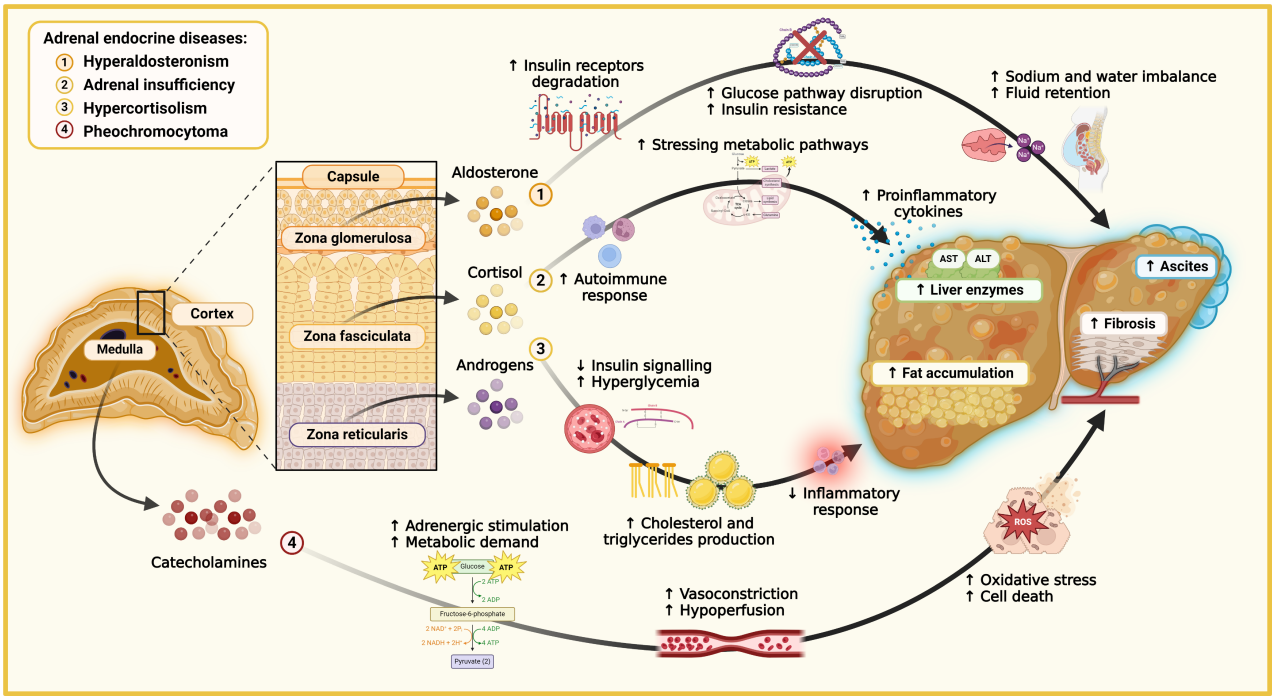

Figure 3 The link between adrenal diseases and liver dysfunction. Molecular pathways connecting adrenal endocrine disorders with liver dysfunction and metabolic complications. In secondary hyperaldosteronism, excess aldosterone from the zona glomerulosa activates mineralocorticoid receptors, leading to sodium and water retention, ascites, and worsening portal hypertension. Aldosterone also increases insulin receptor degradation, contributing to insulin resistance and disrupting glucose homeostasis. In adrenal insufficiency, reduced cortisol from the zona fasciculata impairs anti-inflammatory responses, promoting autoimmune reactions and proinflammatory cytokines like interleukin-6 and tumor necrosis factor-α, which drive liver inflammation and fibrosis. Excess cortisol disrupts insulin signaling pathways in hypercortisolism, causing hyperglycemia, increased cholesterol and triglyceride synthesis, and ectopic hepatic fat accumulation, leading to steatotic liver disease. In pheochromocytoma, excessive catecholamines from the adrenal medulla increase adrenergic stimulation, resulting in lipolysis, oxidative stress, and reactive oxygen species production, causing vasoconstriction, hypoperfusion, and liver cell damage. These combined effects manifest as elevated liver enzymes, ascites formation, and fibrosis. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ATP: Adenosine triphosphate; ROS: Reactive oxygen species; ADP: Adenosine diphosphate; NAD: Nicotinamide adenine dinucleotide.

model study showed that spironolactone alleviated liver damage and portal hypertension by reducing intrahepatic resistance[56].

At the molecular level, aldosterone exerts its effects by binding to the mineralocorticoid receptor (MR) in the renal distal tubules and collecting ducts. This binding initiates a cascade of events that increase the expression of epithelial sodium channel and the sodium-potassium adenosine triphosphatase pump, facilitating sodium reabsorption and potassium excretion. Additionally, aldosterone influences systemic and hepatic inflammation by promoting oxidative stress and fibrosis through MR activation in non-epithelial tissues[55].

In patients with cirrhosis, aldosterone-induced signaling pathways can exacerbate hepatic fibrosis by stimulating hepatic stellate cells and increasing extracellular matrix deposition. Elevated aldosterone levels also downregulate insulin receptor expression and signaling pathways, contributing to insulin resistance by impairing glucose transporter type 4 translocation and reducing glucose uptake in peripheral tissues.

Therefore, therapeutic strategies targeting RAAS activation, such as MR antagonists, are vital for managing complications related to cirrhosis[55].

Adrenal dysfunction: Adrenal and hepatic functions are intricately linked through both metabolic and endocrine pathways. ACLD contributes to adrenal insufficiency, while adrenal dysfunction can, in turn, exacerbate hepatic injury, creating a complex bidirectional relationship.

Adrenal dysfunction also significantly impacts the liver metabolism of medications, potentially increasing the risk of DILI. Elevated catecholamines in pheochromocytoma cause adrenergic stimulation and vasoconstriction in liver blood vessels, resulting in hypoperfusion and liver dysfunction. Eun *et al*[57] report a pheochromocytoma case with rare symptoms, including systemic inflammatory syndrome and abnormal liver tests[58].

In contrast, In ACLD, adrenal insufficiency, often termed "hepato-adrenal syndrome", is a frequent complication. This condition arises from multiple factors, including impaired hypothalamic-pituitary-adrenal axis regulation, reduced hepatic clearance of adrenocorticotropic hormone and corticotropin-releasing hormone, diminished cholesterol synthesis for steroidogenesis, and elevated systemic inflammation. Hepatocyte dysfunction reduces cholesterol availability, which is crucial for cortisol synthesis in the adrenal cortex mediated by enzymes such as *CYP11A1*, 3β-HSD, and *CYP11B1*. Inflammatory cytokines like TNF-α and IL-6 further suppress these enzymes, impairing cortisol production. Simultaneously, decreased synthesis of cortisol-binding globulin (CBG) and albumin limits total serum cortisol levels, making traditional cortisol assays unreliable. In this context, salivary cortisol has emerged as a useful non-invasive marker of free

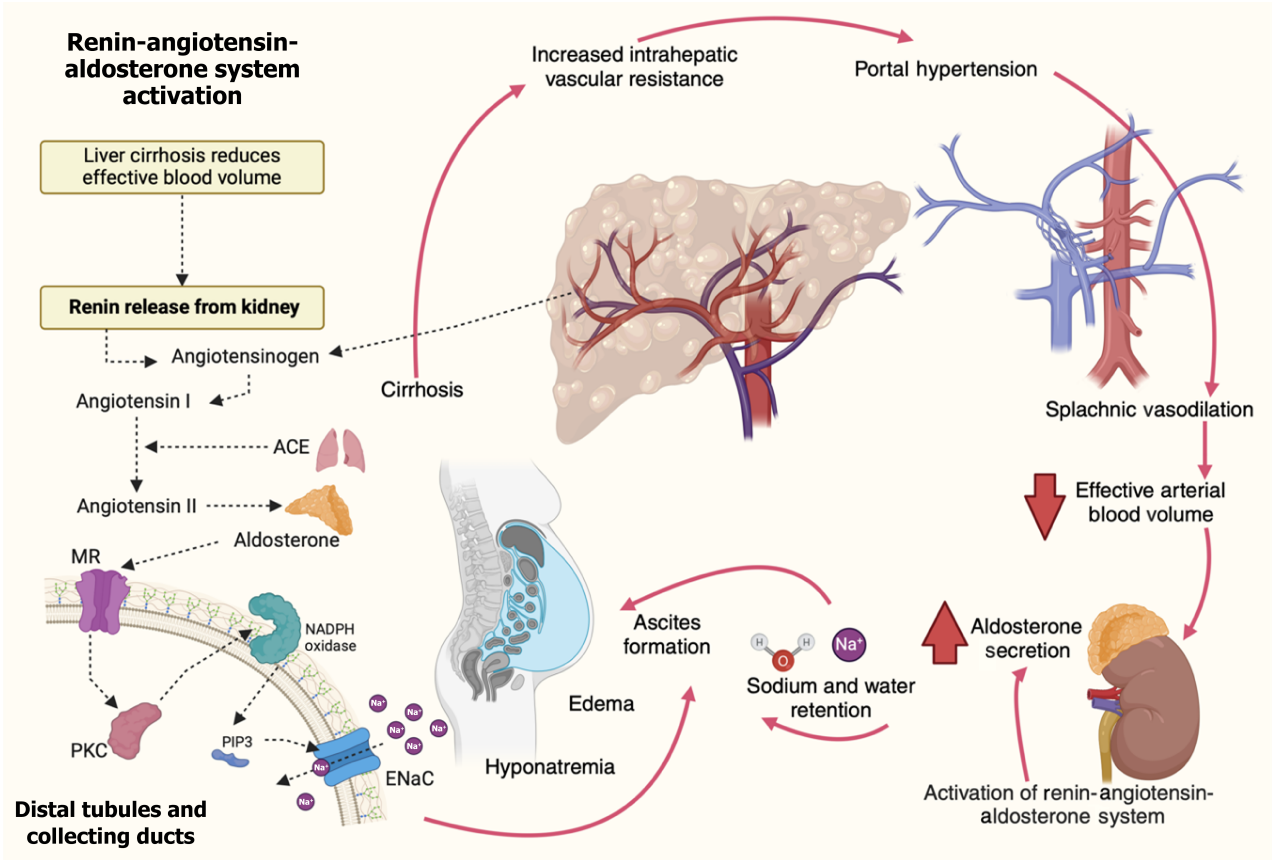

Figure 4 Pathophysiology of secondary hyperaldosteronism in cirrhosis. Molecular mechanisms drive secondary hyperaldosteronism in cirrhosis. Liver fibrosis increases intrahepatic vascular resistance, causing portal hypertension and splanchnic vasodilation. This reduces adequate arterial blood volume despite normal or increased total blood volume. The kidneys respond by activating the renin-angiotensin-aldosterone system (RAAS), triggering renin release, which converts angiotensinogen to angiotensin I. Angiotensin-converting enzyme converts angiotensin I to angiotensin II, stimulating the adrenal glands to secrete aldosterone. Aldosterone promotes sodium and water retention by activating mineralocorticoid receptors in the distal tubules and collecting ducts. This leads to upregulating the epithelial sodium channels (ENaC) and the sodium ion/potassium ion adenosine triphosphate pump. At the molecular level, aldosterone-induced activation of protein kinase C and phosphatidylinositol-3,4,5-trisphosphate (PIP3) enhances ENaC activity. PIP3 serves as a secondary messenger that facilitates the insertion of ENaC into the cell membrane, promoting sodium reabsorption. Oxidative stress *via* nicotinamide adenine dinucleotide phosphate oxidase also potentiates ENaC activation and fluid retention. This cascade leads to ascites formation, edema, and hyponatremia. The cycle of portal hypertension, RAAS activation, and sodium retention perpetuates the development of ascites and exacerbates the complications of cirrhosis. ACE: Angiotensin-converting enzyme; ENaC: Epithelial sodium channels; Na: Sodium; MR: Mineralocorticoid receptor; PIP3: Phosphatidylinositol-3,4,5-trisphosphate; PKC: Protein kinase C.

cortisol[59-61].

Relative adrenal insufficiency occurs in up to 51% of critically ill cirrhotic patients and is associated with increased mortality, hypotension, and septic shock. It may be present with persistent hyponatremia, low mean arterial pressure, and reduced serum sodium. These patients are more prone to bacterial infections, hepatorenal syndrome, and refractory shock. In such cases, hydrocortisone has shown potential to improve shock resolution and survival. Nevertheless, routine corticosteroid replacement in non-critically ill cirrhotic patients remains controversial and should be reserved for select cases with unexplained hypotension or profound fatigue, after excluding other etiologies[59-62].

Evidence from critical care trials and observational studies in cirrhosis suggests this approach may promote earlier shock resolution and improve outcomes in patients with liver failure who require vasopressors[63].

Given these factors, free cortisol levels provide a more accurate assessment of adrenal function in ACLD patients. Salivary cortisol is a promising non-invasive alternative that reflects free cortisol levels and bypasses the variability caused by low CBG and albumin. Determining the optimal cutoff for diagnosing relative adrenal insufficiency in ACLD is challenging due to differences in assay methods, patient conditions, and lack of standardized reference ranges. A complete evaluation of adrenal function should consider clinical presentation and molecular markers to ensure timely diagnosis and management of relative adrenal insufficiency in ACLD patients[50-61].

The impact of sex hormones on liver function and disease progression

Sex hormones, specifically testosterone and estrogens, significantly influence liver function and metabolism (Figure 5). Their regulation is intricately associated with hepatic processes, which control their metabolism, synthesis, conversion, and clearance. Liver dysfunction can disrupt this balance, leading to systemic effects and exacerbating liver pathology[64-66].

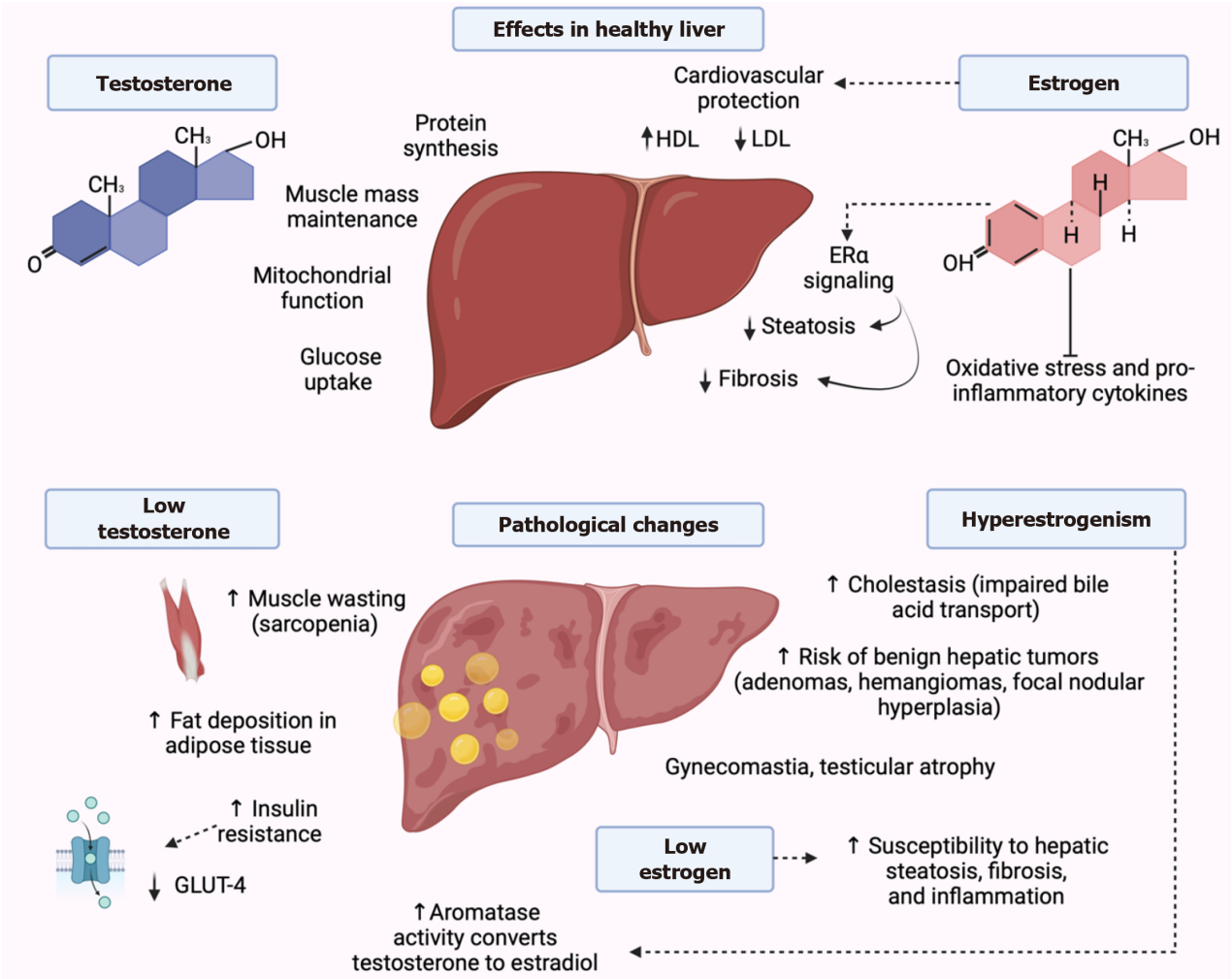

Figure 5 Molecular interplay between sex hormones and liver pathology. Testosterone promotes protein synthesis, mitochondrial function, and glucose uptake *via* androgen receptor activation, supporting muscle mass and metabolic homeostasis. In cirrhosis, reduced testosterone levels lead to sarcopenia, insulin resistance, and increased adiposity. Additionally, elevated aromatase activity enhances the conversion of testosterone to estradiol, contributing to hyperestrogenism. Estrogens, through estrogen receptors (ER) α, ERβ, and G-protein-coupled ER, regulate lipid metabolism, enhance high-density lipoprotein, reduce low-density lipoprotein, and activate antioxidant and anti-inflammatory pathways, protecting against steatosis and fibrosis. However, excess estrogen in advanced liver disease is linked to cholestasis, benign hepatic tumors, and feminizing features such as gynecomastia and testicular atrophy. Low estrogen levels, conversely, are associated with increased hepatic fat accumulation, fibrosis, and inflammation. These interactions emphasize the importance of hormonal balance in maintaining liver health and mitigating progression of liver disease. GLUT-4: Glucose transporter type 4; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; ERα: Estrogen receptor α.

Estrogens contribute to lipid metabolism by upregulating high-density lipoprotein and downregulating low-density lipoprotein levels, thereby offering cardiovascular protection and influencing hepatic fat content[64,65]. These effects are mediated through signaling pathways involving estrogen receptors (ERα and ERβ) and the G-protein-coupled ER. These receptors regulate the transcription of genes involved in lipogenesis, fatty acid oxidation, and cholesterol transport. ERα signaling helps protect against hepatic steatosis and fibrosis by activating pathways that reduce oxidative stress and inhibit pro-inflammatory cytokines such as TNF-α and IL-6[66,67].

In liver disease, sex hormone-binding globulin (SHBG) levels typically increase due to impaired hepatic synthesis and metabolism. SHBG binds to testosterone and estrogens, reducing bioavailable testosterone levels. Therefore, measuring free testosterone levels provides a more accurate assessment of androgen status in patients with chronic liver disease. This decrease in bioavailable testosterone contributes to symptoms such as muscle wasting, insulin resistance, and increased fat deposition.

Additionally, in cirrhosis, aromatase activity within the liver and adipose tissue increases, promoting the conversion of testosterone to estradiol and androstenedione to estrone. This leads to hyperestrogenism, particularly in men, resulting in feminization symptoms such as gynecomastia and testicular atrophy. Elevated estrogen levels can also impair bile acid transporters, contributing to cholestasis and worsening liver function[64,65].

Both nuclear and non-nuclear pathways mediate estrogen's protective effects in the liver. Activation of ERα in hepatocytes helps regulate lipid homeostasis by inhibiting *de novo* lipogenesis and promoting fatty acid oxidation[65,67]. In contrast, estrogen deficiency or dysregulated estrogen signaling increases susceptibility to hepatic steatosis, fibrosis, and inflammation. Studies in ERα-knockout animal models have shown increased liver fat accumulation, insulin resistance, and fibrosis, highlighting estrogen's role in maintaining metabolic homeostasis[66,68].

Conversely, low testosterone levels in chronic liver disease are associated with poor clinical outcomes, including muscle wasting, reduced glucose uptake, and dysregulated lipid metabolism[69,70]. Testosterone supports the expression of genes involved in protein synthesis and mitochondrial function. Therefore, testosterone deficiency exacerbates metabolic dysfunction and accelerates liver disease progression.

Testosterone also significantly influences the progression and severity of various liver diseases, particularly in conditions such as hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) and cirrhosis. Lower testosterone levels have been linked to worse outcomes in these conditions. In HBV-ACLF, reduced levels of testosterone and the free testosterone index are associated with increased disease severity, including higher rates of ascites, hepatic encephalopathy, and overall mortality[65,69].

In patients with cirrhosis, low testosterone levels frequently lead to muscle wasting and increased fat deposition, which further exacerbates liver disease progression. This decline in testosterone results from impaired hepatic synthesis of SHBG, which increases the bioavailability of estrogens and decreases circulating testosterone. Reduced testosterone levels contribute to insulin resistance by impairing glucose uptake in skeletal muscle and promoting lipid accumulation in adipose tissue. Additionally, aromatase activity in adipose tissue and the cirrhotic liver increases the conversion of testosterone to estradiol, exacerbating hyperestrogenism and further disrupting metabolic homeostasis[70-72].

The use of synthetic anabolic steroids, particularly those with 17α-alkylation, can lead to hepatotoxicity by impairing bile flow, causing conditions like cholestasis, peliosis hepatis, and hepatic adenomas[72]. These steroids alter hepatocellular function, resulting in elevated liver enzymes and increased oxidative stress, which can worsen liver damage. Chronic estrogen use also elevates the risk of benign hepatic tumors, such as hepatic adenomas, hemangiomas, and focal nodular hyperplasia, due to estrogen's proliferative effects on hepatic cells[64,72].

In patients with polycystic ovary syndrome (PCOS), insulin resistance, central obesity, and hyperandrogenism significantly increase the prevalence of MASLD. Elevated androgen levels promote hepatic lipid accumulation and systemic inflammation by inducing lipotoxicity and increasing the release of pro-inflammatory cytokines like TNF-α and IL-6. This chronic low-grade inflammation exacerbates hepatic steatosis and fibrosis, linking hyperandrogenism in PCOS to worsening liver function[73,74].

Anterior pituitary gland interactions with the liver

Growth hormone: The anterior pituitary secretes growth hormone (GH), a key regulator of metabolism and liver function. GH stimulates gluconeogenesis during fasting, promotes lipolysis, and triggers IGF-1 production, which supports cell growth and metabolism. However, prolonged GH elevation, as in acromegaly, can lead to insulin resistance, MASLD, oxidative stress, and hepatic fibrosis due to excessive metabolic strain on the liver[75,76]. Nishizawa *et al*[77] studied 69 adults with hypopituitarism and GH deficiency (GHD), all receiving routine hormone replacement. They found that 77% of these patients had nonalcoholic fatty liver disease. GHD patients also had higher levels of AST, ALT, and insulin resistance. After 6-12 months of GH replacement therapy, five patients showed significant improvements in steatosis, fibrosis, and liver enzymes.

Research shows GH reduces MASLD risk by stimulating peripheral lipolysis, breaking down fat in adipose tissue, and inhibiting *de novo* lipogenesis, where the liver synthesizes fatty acids from carbohydrates. GH also aids liver regeneration after injury. Signal transducers and activators of transcription (STAT) 5 activation is key to these protective effects, regulating lipid metabolism and inflammation, thereby protecting the liver and lowering the risk of severe liver diseases, including hepatocellular carcinoma.

Studies in animal models highlight the protective role of GH signaling *via* STAT5 in reducing liver inflammation and fibrosis. Mice with enhanced GH signaling but deficient in STAT5 show increased susceptibility to hepatic steatosis and hepatocellular carcinoma, demonstrating the importance of this pathway in maintaining liver health. The absence of STAT5 results in higher levels of lipogenesis and lipid accumulation in the liver, along with increased activation of tumor-promoting pathways such as STAT3 and c-Jun. These findings illustrate the dual role of GH in liver function: While chronic overexposure to GH can promote liver disease, balanced GH signaling is essential for liver protection and regeneration[76].

Prolactin: It is a polypeptide hormone primarily associated with reproductive functions, but it also plays significant roles in metabolism and immune regulation. The liver metabolizes and clears prolactin from the bloodstream, underscoring its role in maintaining proper hormonal balance. Recent research suggests that prolactin may contribute to developing type 2 diabetes through the prolactin regulatory element-binding protein (PREB), which disrupts glucose deposition in the liver. Overexpression of PREB has been linked to increased secretion of glucagon and glucocorticoids, both of which enhance hepatic gluconeogenesis, contributing to the development of hepatic steatosis and other metabolic disorders[78,79].

In addition to its metabolic effects, prolactin has been shown to modulate the immune system, particularly in the context of chronic hepatitis C. Prolactin enhances IL-2-associated TNF-related apoptosis-inducing ligand expression on natural killer (NK) cells, which are critical for the immune system's ability to control viral infections[69]. In chronic hepatitis C, the immune system's ability to manage viral replication is often impaired, leading to persistent liver inflammation and damage. Prolactin's role in boosting NK cell activity allows for more efficient targeting and destruction of virus-infected hepatocytes, thereby reducing viral load and limiting liver damage[69].

Moreover, prolactin has broader immunoregulatory functions beyond its endocrine role. It influences various immune pathways, contributing to the body's ability to manage chronic infections like hepatitis C. By regulating the balance between pro-inflammatory and anti-inflammatory responses, prolactin helps maintain liver health during chronic illnesses. It is a critical factor in controlling the progression of liver disease and preventing severe outcomes such as cirrhosis or liver failure[80].

ACLD AND ENDOCRINE DYSFUNCTION

ACLD is characterized by extensive liver damage due to fibrosis or inflammation, significantly impacting endocrine function through disrupted hormone metabolism, synthesis, and clearance. Impaired liver function alters the balance of key hormones, leading to clinical manifestations such as hypogonadism, thyroid dysfunction, and glucose metabolism issues[81,82].

Impact of thyroid hormone metabolism

Liver dysfunction can disrupt thyroid hormone homeostasis through multiple interconnected mechanisms, as the liver is essential for thyroid hormone metabolism, transport, and clearance. It plays a pivotal role in the peripheral conversion of T4 into its active form, T3, *via* type 1 deiodinase (D1), and also contributes to hormone conjugation, excretion, and the synthesis of key transport proteins such as thyroxine-binding globulin (TBG) and transthyretin.

In chronic stages like advanced fibrosis or cirrhosis, D1 activity decreases while type 3 deiodinase activity increases, leading to enhanced degradation of T3 and T4 into inactive metabolites such as reverse T3 (rT3). This results in a biochemical profile consistent with euthyroid sick syndrome or non-thyroidal illness syndrome, marked by low T3, elevated rT3, and often normal or low TSH and T4 Levels. These changes are further influenced by inflammatory signals and the activation of hepatic repair pathways, such as the Hedgehog signaling cascade, which affects deiodinase expression and promotes intrahepatic hypothyroidism, even when systemic thyroid hormone levels appear normal[83,84].

Additionally, liver dysfunction alters the production and clearance of binding proteins. Cirrhosis, for instance, can increase TBG levels due to hyperestrogenism, raising total T4 and T3 Levels while leaving free hormone concentrations unchanged or reduced. This can complicate thyroid function interpretation and may necessitate dose adjustments in hypothyroid patients receiving levothyroxine. Furthermore, impaired conjugation and biliary excretion of thyroid hormones and their metabolites in liver disease can exacerbate these hormonal imbalances The severity of liver dysfunction correlates with the extent of thyroid hormone disturbance. In more advanced disease, these changes become more pronounced, with decreased free T3, elevated TSH, and more profound disruptions in hormone binding, metabolism, and clearance[85,86].

Estrogen imbalance and gonadal axis disruption

Chronic liver disease disrupts the metabolism, clearance, and regulation of sex hormones, leading to a hormonal imbalance marked by an elevated estrogen-to-testosterone ratio. Impaired hepatic function alters estrogen metabolism, particularly reducing 2-hydroxylation and increasing 16α-hydroxylation, resulting in increased circulating estrogens. This imbalance is further amplified by portosystemic shunting, which allows unmetabolized estrogens to bypass hepatic clearance, and by enhanced peripheral aromatization of androgens to estrogens in adipose tissue. These mechanisms collectively suppress hypothalamic gonadotropin-releasing hormone and reduce pituitary secretion of luteinizing hormone and follicle-stimulating hormone, culminating in hypogonadotropic hypogonadism. Clinically, men may present with gynecomastia, testicular atrophy, decreased libido, erectile dysfunction, and feminization, while women may experience menstrual irregularities, anovulation, or infertility. Additionally, altered production of SHBG, initially elevated in early liver disease and declining in advanced cirrhosis, further modulates the bioavailability of sex steroids, contributing to endocrine dysfunction in both sexes[81,87]. Malnutrition, prevalent in cirrhosis due to decreased appetite, nutrient malabsorption, and increased metabolic demands, exacerbates hypogonadism by depleting essential nutrients for hormone production[65,82].

Liver-pancreas axis and metabolic impairment

Cirrhosis-related pancreatic dysfunction is linked to gut microbiota changes. Dysbiosis produces harmful metabolites that affect the liver and pancreas, causing inflammation and metabolic issues. Disruptions in short-chain fatty acids and bile acids impair glucose and lipid metabolism, affecting pancreatic hormone secretion, including insulin and glucagon[88]. Grancini *et al*[89] found that in MAFLD, free fatty acids build up in pancreatic islets, while hepatitis C harms beta-cell function through viral toxicity and autoimmune responses. This decline in beta-cell function increases diabetes risk, indicating cirrhotic patients might benefit from thiazolidinediones and incretin-based therapies.

Portal hypertension in cirrhosis can also cause portosystemic shunting, which allows toxins and inflammatory mediators to bypass the liver and accumulate in the bloodstream, adversely affecting pancreatic tissue. This can increase oxidative stress and inflammation in the pancreas, potentially leading to pancreatitis. Additionally, oxidative stress and mitochondrial dysfunction in the pancreas can impair autophagy, leading to cell death and further exacerbating pancreatic injury[88,90]. Pancreatic dysfunction often presents with steatorrhea, malabsorption, and nutrient deficiencies. Management centers on pancreatic enzyme replacement therapy, which should be administered with meals and adjusted based on symptom response to improve digestion, nutritional status, and fat-soluble vitamin levels. Strategies such as splitting enzyme doses during meals, adding acid-suppressing agents if enzyme inactivation is suspected, and addressing bacterial overgrowth can enhance efficacy. Nutritional support is equally essential, emphasizing frequent high-protein meals, alcohol and tobacco avoidance, targeted supplementation, and minimizing fasting to reduce catabolism. In severe cases, enteral nutrition may be required. While current treatments do not reverse pancreatic damage, they focus on symptom relief, nutritional optimization, and complication prevention[91,92].

CONCLUSION

The intricate and bidirectional relationship between the endocrine system and liver function is increasingly recognized as a critical aspect of systemic health. Hormonal imbalances, whether involving the thyroid, pancreas, adrenal glands, parathyroid, or sex hormones, can precipitate or exacerbate liver dysfunction through diverse metabolic and inflammatory mechanisms. At the same time, chronic liver diseases such as ACLD and MASLD profoundly alter endocrine homeostasis by impairing hormone clearance, disrupting feedback regulation, and inducing systemic inflammation. These interactions manifest clinically as insulin resistance, adrenal insufficiency, thyroid dysfunction, and reproductive abnormalities, all of which may accelerate liver injury and complicate management. A comprehensive understanding of these mechanisms is essential for improving diagnostic accuracy and optimizing treatment. Integrating endocrine evaluation into the routine care of patients with liver disease, and vice versa, can enhance outcomes and mitigate long-term complications. Future research should focus on targeted, multidisciplinary interventions that address both hepatic and endocrine dysfunction concurrently, paving the way for more personalized and effective therapeutic strategies.

FOOTNOTES

Author contributions: Vargas-Beltran AM, Armendariz-Pineda SM, Martínez-Sánchez FD, Martinez-Perez C wrote the actual manuscript; Vargas-Beltran AM, Martínez-Sánchez FD were responsible for preparing the figures; Torre A, Cordova-Gallardo J revised and polished the manuscript as co-corresponding authors; Vargas-Beltran AM was responsible for the submission of the current version of the manuscript; All authors have read and approved the final manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Open Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country of origin: Mexico

ORCID number: Andres M Vargas-Beltran 0009-0009-1133-2944; Samantha M Armendariz-Pineda 0009-0009-7933-0507; Froylan D Martínez-Sánchez 0000-0002-2719-1105; Aldo Torre 0000-0002-9299-3075; Jacqueline Cordova-Gallardo 0000-0002-4299-5400.

S-Editor: Fan M
L-Editor: A
P-Editor: Zhang L

REFERENCES

1 **Han HS**, Kang G, Kim JS, Choi BH, Koo SH. Regulation of glucose metabolism from a liver-centric perspective. *Exp Mol Med* 2016; **48**: e218 [*RCA*] [PMID: 26964834 DOI: 10.1038/emm.2015.122] [FullText] [Full Text(PDF)]
2 **Robinson MW**, Harmon C, O'Farrelly C. Liver immunology and its role in inflammation and homeostasis. *Cell Mol Immunol* 2016; **13**: 267-276 [*RCA*] [PMID: 27063467 DOI: 10.1038/cmi.2016.3] [FullText] [Full Text(PDF)]
3 **Marino L**, Kim A, Ni B, Celi FS. Thyroid hormone action and liver disease, a complex interplay. *Hepatology* 2025; **81**: 651-669 [*RCA*] [PMID: 37535802 DOI: 10.1097/HEP.0000000000000551] [FullText]
4 **Kumar KV**, Pawah AK, Manrai M. Occult endocrine dysfunction in patients with cirrhosis of liver. *J Family Med Prim Care* 2016; **5**: 576-580 [*RCA*] [PMID: 28217586 DOI: 10.4103/2249-4863.197293] [FullText] [Full Text(PDF)]
5 **Bano A**, Chaker L, Plompen EP, Hofman A, Dehghan A, Franco OH, Janssen HL, Darwish Murad S, Peeters RP. Thyroid Function and the Risk of Nonalcoholic Fatty Liver Disease: The Rotterdam Study. *J Clin Endocrinol Metab* 2016; **101**: 3204-3211 [*RCA*] [PMID: 27270473 DOI: 10.1210/jc.2016-1300] [FullText]
6 **Malik R**, Hodgson H. The relationship between the thyroid gland and the liver. *QJM* 2002; **95**: 559-569 [*RCA*] [PMID: 12205333 DOI: 10.1093/qjmed/95.9.559] [FullText]
7 **Lecureux L**, Dieter MZ, Nelson DM, Watson L, Wong H, Gemzik B, Klaassen CD, Lehman-McKeeman LD. Hepatobiliary disposition of thyroid hormone in Mrp2-deficient TR- rats: reduced biliary excretion of thyroxine glucuronide does not prevent xenobiotic-induced hypothyroidism. *Toxicol Sci* 2009; **108**: 482-491 [*RCA*] [PMID: 19211616 DOI: 10.1093/toxsci/kfp026] [FullText]
8 **Ajala MO**, Ogunro PS, Fasanmade OA. Relationship between liver function tests and thyroid hormones in thyroid disorders. *Niger Postgrad Med J* 2013; **20**: 188-192 [*RCA*] [PMID: 24287748] [FullText]
9 **Laukkarinen J**, Sand J, Autio V, Nordback I. Bile duct stone procedures are more frequent in patients with hypothyroidism. A large, registry-based, cohort study in Finland. *Scand J Gastroenterol* 2010; **45**: 70-74 [*RCA*] [PMID: 20030579 DOI: 10.3109/00365520903386721] [Full Text]
10 **Zafar Y**, Suddaby SR, Shafiq M. Hypothyroidism Manifesting as a Combination of Ascites and Malnutrition Requiring Total Parenteral Nutrition: A Unique Presentation. *Cureus* 2019; **11**: e5338 [*RCA*] [PMID: 31598444 DOI: 10.7759/cureus.5338] [FullText] [Full Text(PDF)]
11 **Guo Z**, Li M, Han B, Qi X. Association of non-alcoholic fatty liver disease with thyroid function: A systematic review and meta-analysis. *Dig Liver Dis* 2018; **50**: 1153-1162 [*RCA*] [PMID: 30224316 DOI: 10.1016/j.dld.2018.08.012] [FullText]

12 **Hatziagelaki E**, Paschou SA, Schön M, Psaltopoulou T, Roden M. NAFLD and thyroid function: pathophysiological and therapeutic considerations. *Trends Endocrinol Metab* 2022; **33**: 755-768 [*RCA*] [PMID: 36171155 DOI: 10.1016/j.tem.2022.08.001] [FullText]

13 **Kowalik MA**, Columbano A, Perra A. Thyroid Hormones, Thyromimetics and Their Metabolites in the Treatment of Liver Disease. *Front Endocrinol (Lausanne)* 2018; **9**: 382 [*RCA*] [PMID: 30042736 DOI: 10.3389/fendo.2018.00382] [FullText] [Full Text(PDF)]

14 **Wang R**, Tan J, Zhang G, Zheng W, Li C. Risk factors of hepatic dysfunction in patients with Graves' hyperthyroidism and the efficacy of 131iodine treatment. *Medicine (Baltimore)* 2017; **96**: e6035 [*RCA*] [PMID: 28151911 DOI: 10.1097/MD.0000000000006035] [FullText] [Full Text(PDF)]

15 **Opoku-Akyeampong NAAS**, Agyei-Nkansah A, Yorke E. Liver dysfunction associated with hyperthyroidism: Lessons from 2 Case reports. *Clin Case Rep* 2021; **9**: e04067 [*RCA*] [PMID: 34136225 DOI: 10.1002/ccr3.4067] [FullText] [Full Text(PDF)]

16 **Hayat MH**, Moazzam Z, Ziogas IA, Yousaf A, Hayat M. Thyroid Storm Presenting as Acute Liver Failure in a Patient with Graves' Disease. *Cureus* 2020; **12**: e10333 [*RCA*] [PMID: 33052294 DOI: 10.7759/cureus.10333] [FullText] [Full Text(PDF)]

17 **Scappaticcio L**, Longo M, Maiorino MI, Pernice V, Caruso P, Esposito K, Bellastella G. Abnormal Liver Blood Tests in Patients with Hyperthyroidism: Systematic Review and Meta-Analysis. *Thyroid* 2021; **31**: 884-894 [*RCA*] [PMID: 33327837 DOI: 10.1089/thy.2020.0715] [FullText]

18 **Liu X**, Xu B, Zeng Y, Chen P, Wang Y. Case report: Severe cholestatic jaundice associated with hyperthyroidism treated with methimazole. *Medicine (Baltimore)* 2023; **102**: e35972 [*RCA*] [PMID: 37960740 DOI: 10.1097/MD.0000000000035972] [FullText]

19 **Zeng B**, Yuan L, Chu J, Yang Y, Lin S. Challenges in early identification of causes and treatment of cholestasis in patients with hyperthyroidism: a case report and literature review. *J Int Med Res* 2020; **48**: 300060519891018 [*RCA*] [PMID: 31840543 DOI: 10.1177/0300060519891018] [FullText] [Full Text(PDF)]

20 **Heidari R**, Niknahad H, Jamshidzadeh A, Abdoli N. Factors affecting drug-induced liver injury: antithyroid drugs as instances. *Clin Mol Hepatol* 2014; **20**: 237-248 [*RCA*] [PMID: 25320726 DOI: 10.3350/cmh.2014.20.3.237] [FullText] [Full Text(PDF)]

21 **Carrion AF**, Czul F, Arosemena LR, Selvaggi G, Garcia MT, Tekin A, Tzakis AG, Martin P, Ghanta RK. Propylthiouracil-induced acute liver failure: role of liver transplantation. *Int J Endocrinol* 2010; **2010**: 910636 [*RCA*] [PMID: 21234410 DOI: 10.1155/2010/910636] [FullText] [Full Text(PDF)]

22 **He Q**, Li M, Ji P, Zheng A, Yao L, Zhu X, Shin JG, Lauschke VM, Han B, Xiang X. Comparison of drug-induced liver injury risk between propylthiouracil and methimazole: A quantitative systems toxicology approach. *Toxicol Appl Pharmacol* 2024; **491**: 117064 [*RCA*] [PMID: 39122118 DOI: 10.1016/j.taap.2024.117064] [FullText]

23 **Piantanida E**, Ippolito S, Gallo D, Masiello E, Premoli P, Cusini C, Rosetti S, Sabatino J, Segato S, Trimarchi F, Bartalena L, Tanda ML. The interplay between thyroid and liver: implications for clinical practice. *J Endocrinol Invest* 2020; **43**: 885-899 [*RCA*] [PMID: 32166702 DOI: 10.1007/s40618-020-01208-6] [FullText]

24 **Luo Z**, Lei Y, Zeng L, Chen X, Liu S, Zhang Q. Iodine-131 intervention in hyperthyroidism with hepatic insufficiency: Metabolomic evaluation. *Biomed Pharmacother* 2024; **173**: 116300 [*RCA*] [PMID: 38430629 DOI: 10.1016/j.biopha.2024.116300] [FullText]

25 **Zhang Q**, Guan Y, Xiang T, Liu S, Chen Q, Zhang Q. Combination of Molecular Adsorbent Recirculating System and Radioiodine for the Treatment of Concurrent Hyperthyroidism and Severe Liver Dysfunction: A Retrospective Cohort Study. *Endocr Pract* 2017; **23**: 141-148 [*RCA*] [PMID: 27819764 DOI: 10.4158/EP161417.OR] [FullText]

26 **Jaroenlapnopparat A**, Rittiphairoj T, Chaisidhivej N, Walker B, Charoenngam N. High parathyroid hormone level as a marker of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: A systematic review and meta-analysis. *Diabetes Metab Syndr* 2023; **17**: 102827 [*RCA*] [PMID: 37451113 DOI: 10.1016/j.dsx.2023.102827] [FullText]

27 **Malespin M**, Nassri A. Endocrine Diseases and the Liver: An Update. *Clin Liver Dis* 2019; **23**: 233-246 [*RCA*] [PMID: 30947874 DOI: 10.1016/j.cld.2018.12.006] [FullText]

28 **Hartl L**, Schwarz M, Simbrunner B, Jachs M, Wolf P, Bauer DJM, Scheiner B, Balcar L, Semmler G, Hofer BS, Dominik N, Marculescu R, Trauner M, Mandorfer M, Reiberger T. Insulin-like growth factor-1 in cirrhosis is linked to hepatic dysfunction and fibrogenesis and predicts liver-related mortality. *Aliment Pharmacol Ther* 2025; **61**: 88-98 [*RCA*] [PMID: 39305115 DOI: 10.1111/apt.18289] [FullText]

29 **Chondrogianni ME**, Kyrou I, Androutsakos T, Flessa CM, Menenakos E, Chatha KK, Aranan Y, Papavassiliou AG, Kassi E, Randeva HS. Anti-osteoporotic treatments in the era of non-alcoholic fatty liver disease: friend or foe. *Front Endocrinol (Lausanne)* 2024; **15**: 1344376 [*RCA*] [PMID: 38524631 DOI: 10.3389/fendo.2024.1344376] [FullText] [Full Text(PDF)]

30 **Chaudhury CS**, Mee T, Chairez C, McLaughlin M, Silk R, Gross C, Kattakuzhy S, Rosenthal E, Kottilil S, Stanley TL, Hadigan C. Testosterone in Men With Chronic Hepatitis C Infection and After Hepatitis C Viral Clearance. *Clin Infect Dis* 2019; **69**: 571-576 [*RCA*] [PMID: 30715229 DOI: 10.1093/cid/ciy965] [FullText]

31 **Vachliotis ID**, Polyzos SA. Osteoprotegerin/Receptor Activator of Nuclear Factor-Kappa B Ligand/Receptor Activator of Nuclear Factor-Kappa B Axis in Obesity, Type 2 Diabetes Mellitus, and Nonalcoholic Fatty Liver Disease. *Curr Obes Rep* 2023; **12**: 147-162 [*RCA*] [PMID: 37208545 DOI: 10.1007/s13679-023-00505-4] [FullText]

32 **Richter MM**, Galsgaard KD, Elmelund E, Knop FK, Suppli MP, Holst JJ, Winther-Sørensen M, Kjeldsen SAS, Wewer Albrechtsen NJ. The Liver-α-Cell Axis in Health and in Disease. *Diabetes* 2022; **71**: 1852-1861 [*RCA*] [PMID: 35657688 DOI: 10.2337/dbi22-0004] [FullText] [Full Text(PDF)]

33 **Rigal S**, Casas B, Kanebratt KP, Wennberg Huldt C, Magnusson LU, Müllers E, Karlsson F, Clausen M, Hansson SF, Leonard L, Cairns J, Jansson Löfmark R, Ämmälä C, Marx U, Gennemark P, Cedersund G, Andersson TB, Vilén LK. Normoglycemia and physiological cortisone level maintain glucose homeostasis in a pancreas-liver microphysiological system. *Commun Biol* 2024; **7**: 877 [*RCA*] [PMID: 39025915 DOI: 10.1038/s42003-024-06514-w] [FullText]

34 **Sancar G**, Birkenfeld AL. The role of adipose tissue dysfunction in hepatic insulin resistance and T2D. *J Endocrinol* 2024; **262**: e240115 [*RCA*] [PMID: 38967989 DOI: 10.1530/JOE-24-0115] [FullText]

35 **Medina-Urrutia AX**, Jorge-Galarza E, El Hafidi M, Reyes-Barrera J, Páez-Arenas A, Masso-Rojas FA, Martínez-Sánchez FD, López-Uribe ÁR, González-Salazar MDC, Torres-Tamayo M, Juárez-Rojas JG. Effect of dietary chia supplementation on glucose metabolism and adipose tissue function markers in non-alcoholic fatty liver disease subjects. *Nutr Hosp* 2022; **39**: 1280-1288 [*RCA*] [PMID: 36250773 DOI: 10.20960/nh.04084] [FullText]

36 **Huang P**, Zhu Y, Qin J. Research advances in understanding crosstalk between organs and pancreatic β-cell dysfunction. *Diabetes Obes Metab* 2024; **26**: 4147-4164 [*RCA*] [PMID: 39044309 DOI: 10.1111/dom.15787] [FullText]

37 **Regnell SE**, Lernmark Å. Hepatic steatosis in type 1 diabetes. *Rev Diabet Stud* 2011; **8**: 454-467 [*RCA*] [PMID: 22580727 DOI:

10.1900/RDS.2011.8.454] [FullText]
38 **Martínez-Sánchez FD**, Vargas-Abonce VP, Rocha-Haro A, Flores-Cardenas R, Fernández-Barrio M, Guerrero-Castillo AP, Meza-Arana CE, Gulias-Herrero A, Gómez-Sámano MÁ. Visceral adiposity index is associated with insulin resistance, impaired insulin secretion, and β-cell dysfunction in subjects at risk for type 2 diabetes. *Diabetes Epidemiol Manag* 2021; **2**: 100013 [DOI: 10.1016/j.deman.2021.100013] [FullText]
39 **Rinella ME**, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, Kleiner DE, Loomba R. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 2023; **77**: 1797-1835 [*RCA*] [PMID: 36727674 DOI: 10.1097/HEP.0000000000000323] [FullText]
40 **American Diabetes Association Professional Practice Committee**. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes-2025. *Diabetes Care* 2025; **48**: S59-S85 [*RCA*] [PMID: 39651988 DOI: 10.2337/dc25-S004] [FullText]
41 **Wang Y**, Lin Z, Wan H, Zhang W, Xia F, Chen Y, Chen X, Wang C, Chen C, Wang N, Lu Y. Glucagon is associated with NAFLD inflammatory progression in type 2 diabetes, not with NAFLD fibrotic progression. *Eur J Gastroenterol Hepatol* 2021; **33**: e818-e823 [*RCA*] [PMID: 34402473 DOI: 10.1097/MEG.0000000000002269] [FullText] [Full Text(PDF)]
42 **Ullah A**, Chen Y, Singla RK, Cao D, Shen B. Exploring cytokines dynamics: Uncovering therapeutic concepts for metabolic disorders in postmenopausal women- diabetes, metabolic bone diseases, and non-alcohol fatty liver disease. *Ageing Res Rev* 2024; **101**: 102505 [*RCA*] [PMID: 39307315 DOI: 10.1016/j.arr.2024.102505] [FullText]
43 **Caputo T**, Gilardi F, Desvergne B. From chronic overnutrition to metaflammation and insulin resistance: adipose tissue and liver contributions. *FEBS Lett* 2017; **591**: 3061-3088 [*RCA*] [PMID: 28677122 DOI: 10.1002/1873-3468.12742] [FullText]
44 **Lackey DE**, Olefsky JM. Regulation of metabolism by the innate immune system. *Nat Rev Endocrinol* 2016; **12**: 15-28 [*RCA*] [PMID: 26553134 DOI: 10.1038/nrendo.2015.189] [FullText]
45 **Püschel GP**, Klauder J, Henkel J. Macrophages, Low-Grade Inflammation, Insulin Resistance and Hyperinsulinemia: A Mutual Ambiguous Relationship in the Development of Metabolic Diseases. *J Clin Med* 2022; **11**: 4358 [*RCA*] [PMID: 35955975 DOI: 10.3390/jcm11154358] [FullText] [Full Text(PDF)]
46 **Ciochina M**, Balaban DV, Manucu G, Jinga M, Gheorghe C. The Impact of Pancreatic Exocrine Diseases on the β-Cell and Glucose Metabolism-A Review with Currently Available Evidence. *Biomolecules* 2022; **12**: 618 [*RCA*] [PMID: 35625546 DOI: 10.3390/biom12050618] [FullText] [Full Text(PDF)]
47 **Stefan N**, Schick F, Birkenfeld AL, Häring HU, White MF. The role of hepatokines in NAFLD. *Cell Metab* 2023; **35**: 236-252 [*RCA*] [PMID: 36754018 DOI: 10.1016/j.cmet.2023.01.006] [FullText]
48 **Gangneux C**, Daveau M, Hiron M, Derambure C, Papaconstantinou J, Salier JP. The inflammation-induced down-regulation of plasma Fetuin-A (alpha2HS-Glycoprotein) in liver results from the loss of interaction between long C/EBP isoforms at two neighbouring binding sites. *Nucleic Acids Res* 2003; **31**: 5957-5970 [*RCA*] [PMID: 14530444 DOI: 10.1093/nar/gkg788] [FullText]
49 **Kharb S**, Garg MK, Puri P, Nandi B, Brar KS, Gundgurthi A, Pandit A. Assessment of adrenal function in liver diseases. *Indian J Endocrinol Metab* 2013; **17**: 465-471 [*RCA*] [PMID: 23869304 DOI: 10.4103/2230-8210.111643] [FullText] [Full Text(PDF)]
50 **Tarantino G**, Finelli C. Pathogenesis of hepatic steatosis: the link between hypercortisolism and non-alcoholic fatty liver disease. *World J Gastroenterol* 2013; **19**: 6735-6743 [*RCA*] [PMID: 24187449 DOI: 10.3748/wjg.v19.i40.6735] [FullText] [Full Text(PDF)]
51 **Rockall AG**, Sohaib SA, Evans D, Kaltsas G, Isidori AM, Monson JP, Besser GM, Grossman AB, Reznek RH. Hepatic steatosis in Cushing's syndrome: a radiological assessment using computed tomography. *Eur J Endocrinol* 2003; **149**: 543-548 [*RCA*] [PMID: 14640995 DOI: 10.1530/eje.0.1490543] [FullText]
52 **Wentworth BJ**, Siragy HM. Adrenal Insufficiency in Cirrhosis. *J Endocr Soc* 2022; **6**: bvac115 [*RCA*] [PMID: 36033971 DOI: 10.1210/jendso/bvac115] [FullText] [Full Text(PDF)]
53 **Karagiannis AK**, Nakouti T, Pipili C, Cholongitas E. Adrenal insufficiency in patients with decompensated cirrhosis. *World J Hepatol* 2015; **7**: 1112-1124 [*RCA*] [PMID: 26052400 DOI: 10.4254/wjh.v7.i8.1112] [FullText] [Full Text(PDF)]
54 **Trifan A**, Chiriac S, Stanciu C. Update on adrenal insufficiency in patients with liver cirrhosis. *World J Gastroenterol* 2013; **19**: 445-456 [*RCA*] [PMID: 23382623 DOI: 10.3748/wjg.v19.i4.445] [FullText] [Full Text(PDF)]
55 **Quiroz-Aldave JE**, Gamarra-Osorio ER, Durand-Vásquez MDC, Rafael-Robles LDP, Gonzáles-Yovera JG, Quispe-Flores MA, Concepción-Urteaga LA, Román-González A, Paz-Ibarra J, Concepción-Zavaleta MJ. From liver to hormones: The endocrine consequences of cirrhosis. *World J Gastroenterol* 2024; **30**: 1073-1095 [*RCA*] [PMID: 38577191 DOI: 10.3748/wjg.v30.i9.1073] [FullText] [Full Text(PDF)]
56 **Luo W**, Meng Y, Ji HL, Pan CQ, Huang S, Yu CH, Xiao LM, Cui K, Ni SY, Zhang ZS, Li X. Spironolactone lowers portal hypertension by inhibiting liver fibrosis, ROCK-2 activity and activating NO/PKG pathway in the bile-duct-ligated rat. *PLoS One* 2012; **7**: e34230 [*RCA*] [PMID: 22479572 DOI: 10.1371/journal.pone.0034230] [FullText] [Full Text(PDF)]
57 **Eun CR**, Ahn JH, Seo JA, Kim NH. Pheochromocytoma with markedly abnormal liver function tests and severe leukocytosis. *Endocrinol Metab (Seoul)* 2014; **29**: 83-90 [*RCA*] [PMID: 24741459 DOI: 10.3803/EnM.2014.29.1.83] [FullText] [Full Text(PDF)]
58 **Lelou E**, Corlu A, Nesseler N, Rauch C, Mallédant Y, Seguin P, Aninat C. The Role of Catecholamines in Pathophysiological Liver Processes. *Cells* 2022; **11**: 1021 [*RCA*] [PMID: 35326472 DOI: 10.3390/cells11061021] [FullText] [Full Text(PDF)]
59 **Fernández J**, Escorsell A, Zabalza M, Felipe V, Navasa M, Mas A, Lacy AM, Ginès P, Arroyo V. Adrenal insufficiency in patients with cirrhosis and septic shock: Effect of treatment with hydrocortisone on survival. *Hepatology* 2006; **44**: 1288-1295 [*RCA*] [PMID: 17058239 DOI: 10.1002/hep.21352] [FullText]
60 **Fede G**, Spadaro L, Tomaselli T, Privitera G, Piro S, Rabuazzo AM, Sigalas A, Xirouchakis E, O'Beirne J, Garcovich M, Tsochatzis E, Purrello F, Burroughs AK. Assessment of adrenocortical reserve in stable patients with cirrhosis. *J Hepatol* 2011; **54**: 243-250 [*RCA*] [PMID: 21056503 DOI: 10.1016/j.jhep.2010.06.034] [FullText]
61 **Theocharidou E**, Giouleme O, Anastasiadis S, Markopoulou A, Pagourelias E, Vassiliadis T, Fotoglidis A, Agorastou P, Slavakis A, Balaska A, Kouskoura MG, Gossios TD, Karagiannis A, Mantzoros CS. Free Cortisol Is a More Accurate Marker for Adrenal Function and Does Not Correlate with Renal Function in Cirrhosis. *Dig Dis Sci* 2019; **64**: 1686-1694 [*RCA*] [PMID: 30659471 DOI: 10.1007/s10620-019-5460-x] [FullText]
62 **Tsai MH**, Peng YS, Chen YC, Liu NJ, Ho YP, Fang JT, Lien JM, Yang C, Chen PC, Wu CS. Adrenal insufficiency in patients with cirrhosis, severe sepsis and septic shock. *Hepatology* 2006; **43**: 673-681 [*RCA*] [PMID: 16557538 DOI: 10.1002/hep.21101] [FullText]
63 **Marik PE**, Gayowski T, Starzl TE; Hepatic Cortisol Research and Adrenal Pathophysiology Study Group. The hepatoadrenal syndrome: a common yet unrecognized clinical condition. *Crit Care Med* 2005; **33**: 1254-1259 [*RCA*] [PMID: 15942340 DOI:

10.1097/01.ccm.0000164541.12106.57] [FullText]
64 **Kasarinaite A**, Sinton M, Saunders PTK, Hay DC. The Influence of Sex Hormones in Liver Function and Disease. *Cells* 2023; **12**: 1604 [*RCA*] [PMID: 37371074 DOI: 10.3390/cells12121604] [FullText] [Full Text(PDF)]
65 **Palmisano BT**, Zhu L, Stafford JM. Role of Estrogens in the Regulation of Liver Lipid Metabolism. *Adv Exp Med Biol* 2017; **1043**: 227-256 [*RCA*] [PMID: 29224098 DOI: 10.1007/978-3-319-70178-3_12] [FullText]
66 **Chambliss KL**, Barrera J, Umetani M, Umetani J, Kim SH, Madak-Erdogan Z, Huang L, Katzenellenbogen BS, Katzenellenbogen JA, Mineo C, Shaul PW. Nonnuclear Estrogen Receptor Activation Improves Hepatic Steatosis in Female Mice. *Endocrinology* 2016; **157**: 3731-3741 [*RCA*] [PMID: 27552247 DOI: 10.1210/en.2015-1629] [FullText]
67 **Hart-Unger S**, Arao Y, Hamilton KJ, Lierz SL, Malarkey DE, Hewitt SC, Freemark M, Korach KS. Hormone signaling and fatty liver in females: analysis of estrogen receptor α mutant mice. *Int J Obes (Lond)* 2017; **41**: 945-954 [*RCA*] [PMID: 28220039 DOI: 10.1038/ijo.2017.50] [FullText] [Full Text(PDF)]
68 **Matic M**, Bryzgalova G, Gao H, Antonson P, Humire P, Omoto Y, Portwood N, Pramfalk C, Efendic S, Berggren PO, Gustafsson JÅ, Dahlman-Wright K. Estrogen signalling and the metabolic syndrome: targeting the hepatic estrogen receptor alpha action. *PLoS One* 2013; **8**: e57458 [*RCA*] [PMID: 23451233 DOI: 10.1371/journal.pone.0057458] [FullText] [Full Text(PDF)]
69 **Huang Y**, Yan D, Zhang H, Lou B, Yan R, Yao Y, Dong M, Yang D, Lv F, Chen Y. Lower testosterone levels predict increasing severity and worse outcomes of hepatitis B virus-related acute-on-chronic liver failure in males. *BMC Gastroenterol* 2021; **21**: 457 [*RCA*] [PMID: 34872528 DOI: 10.1186/s12876-021-01993-1] [FullText] [Full Text(PDF)]
70 **Kim SM**, Yalamanchi S, Dobs AS. Male Hypogonadism and Liver Disease. In: Winters S, Huhtaniemi I (editors). Male Hypogonadism. Humana Press, Cham, 2017: 219-234 [DOI: 10.1007/978-3-319-53298-1_11] [FullText]
71 **Deng N**, Mallepally N, Peng FB, Kanji A, Marcelli M, Hernaez R. Serum testosterone levels and testosterone supplementation in cirrhosis: A systematic review. *Liver Int* 2021; **41**: 2358-2370 [*RCA*] [PMID: 33966337 DOI: 10.1111/liv.14938] [FullText]
72 **Niedfeldt MW**. Anabolic Steroid Effect on the Liver. *Curr Sports Med Rep* 2018; **17**: 97-102 [*RCA*] [PMID: 29521706 DOI: 10.1249/JSR.0000000000000467] [FullText]
73 **Purwar A**, Nagpure S. Insulin Resistance in Polycystic Ovarian Syndrome. *Cureus* 2022; **14**: e30351 [*RCA*] [PMID: 36407241 DOI: 10.7759/cureus.30351] [FullText] [Full Text(PDF)]
74 **Chen MJ**, Ho HN. Hepatic manifestations of women with polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol* 2016; **37**: 119-128 [*RCA*] [PMID: 27107966 DOI: 10.1016/j.bpobgyn.2016.03.003] [FullText]
75 **Ma IL**, Stanley TL. Growth hormone and nonalcoholic fatty liver disease. *Immunometabolism (Cobham)* 2023; **5**: e00030 [*RCA*] [PMID: 37520312 DOI: 10.1097/IN9.0000000000000030] [FullText]
76 **Friedbichler K**, Themanns M, Mueller KM, Schlederer M, Kornfeld JW, Terracciano LM, Kozlov AV, Haindl S, Kenner L, Kolbe T, Mueller M, Snibson KJ, Heim MH, Moriggl R. Growth-hormone-induced signal transducer and activator of transcription 5 signaling causes gigantism, inflammation, and premature death but protects mice from aggressive liver cancer. *Hepatology* 2012; **55**: 941-952 [*RCA*] [PMID: 22031092 DOI: 10.1002/hep.24765] [FullText]
77 **Nishizawa H**, Iguchi G, Murawaki A, Fukuoka H, Hayashi Y, Kaji H, Yamamoto M, Suda K, Takahashi M, Seo Y, Yano Y, Kitazawa R, Kitazawa S, Koga M, Okimura Y, Chihara K, Takahashi Y. Nonalcoholic fatty liver disease in adult hypopituitary patients with GH deficiency and the impact of GH replacement therapy. *Eur J Endocrinol* 2012; **167**: 67-74 [*RCA*] [PMID: 22535644 DOI: 10.1530/EJE-12-0252] [Full Text]
78 **Park JM**, Kim MY, Kim TH, Min DK, Yang GE, Ahn YH. Prolactin regulatory element-binding (PREB) protein regulates hepatic glucose homeostasis. *Biochim Biophys Acta Mol Basis Dis* 2018; **1864**: 2097-2107 [*RCA*] [PMID: 29601978 DOI: 10.1016/j.bbadis.2018.03.024] [Full Text]
79 **Zhang J**, Guan J, Tang X, Xu J. Prolactin is a Key Factor for Nonalcoholic Fatty Liver Disease in Obese Children. *Horm Metab Res* 2023; **55**: 251-255 [*RCA*] [PMID: 36849108 DOI: 10.1055/a-2043-1044] [FullText] [Full Text(PDF)]
80 **Medel MLH**, Reyes GG, Porras LM, Bernal AR, Luna JS, Garcia AP, Cordova J, Parra A, Mummidi S, Kershenobich D, Hernández J. Prolactin Induces IL-2 Associated TRAIL Expression on Natural Killer Cells from Chronic Hepatitis C Patients In vivo and In vitro. *Endocr Metab Immune Disord Drug Targets* 2019; **19**: 975-984 [*RCA*] [PMID: 30520386 DOI: 10.2174/1871530319666181206125545] [FullText]
81 **Di Ciaula A**, Christidis G, Krawczyk M, Lammert F, Portincasa P. Impact of Endocrine Disorders on the Liver. In: Portincasa P, Frühbeck G, Nathoe HM (editors). Endocrinology and Systemic Diseases. Springer, Cham, 2020: 157-177
82 **Marik PE**. Adrenal-exhaustion syndrome in patients with liver disease. *Intensive Care Med* 2006; **32**: 275-280 [*RCA*] [PMID: 16432671 DOI: 10.1007/s00134-005-0005-5] [FullText]
83 **Bohinc BN**, Michelotti G, Xie G, Pang H, Suzuki A, Guy CD, Piercy D, Kruger L, Swiderska-Syn M, Machado M, Pereira T, Zavacki AM, Abdelmalek M, Diehl AM. Repair-related activation of hedgehog signaling in stromal cells promotes intrahepatic hypothyroidism. *Endocrinology* 2014; **155**: 4591-4601 [*RCA*] [PMID: 25121996 DOI: 10.1210/en.2014-1302] [FullText]
84 **Bebars GM**, Sayed MA, Hamdy L, Abdel Aziz RA. Effect of acute and chronic liver diseases on the thyroid function in children. *BMC Pediatr* 2021; **21**: 361 [*RCA*] [PMID: 34433432 DOI: 10.1186/s12887-021-02816-8] [FullText] [Full Text(PDF)]
85 **Benvenga S**, Capodicasa G, Perelli S, Ferrari SM, Fallahi P, Antonelli A. Increased Requirement of Replacement Doses of Levothyroxine Caused by Liver Cirrhosis. *Front Endocrinol (Lausanne)* 2018; **9**: 150 [*RCA*] [PMID: 29720960 DOI: 10.3389/fendo.2018.00150] [FullText] [Full Text(PDF)]
86 **Zumoff B**, Fishman J, Gallagher TF, Hellman L. Estradiol metabolism in cirrhosis. *J Clin Invest* 1968; **47**: 20-25 [*RCA*] [PMID: 16695941 DOI: 10.1172/JCI105709] [FullText]
87 **Velissaris D**, Karanikolas M, Kalogeropoulos A, Solomou E, Polychronopoulos P, Thomopoulos K, Labropoulou-Karatza C. Pituitary hormone circadian rhythm alterations in cirrhosis patients with subclinical hepatic encephalopathy. *World J Gastroenterol* 2008; **14**: 4190-4195 [*RCA*] [PMID: 18636665 DOI: 10.3748/wjg.14.4190] [FullText] [Full Text(PDF)]
88 **Marroncini G**, Naldi L, Martinelli S, Amedei A. Gut-Liver-Pancreas Axis Crosstalk in Health and Disease: From the Role of Microbial Metabolites to Innovative Microbiota Manipulating Strategies. *Biomedicines* 2024; **12**: 1398 [*RCA*] [PMID: 39061972 DOI: 10.3390/biomedicines12071398] [FullText] [Full Text(PDF)]
89 **Grancini V**, Trombetta M, Lunati ME, Zimbalatti D, Boselli ML, Gatti S, Donato MF, Resi V, D'Ambrosio R, Aghemo A, Pugliese G, Bonadonna RC, Orsi E. Contribution of β-cell dysfunction and insulin resistance to cirrhosis-associated diabetes: Role of severity of liver disease. *J Hepatol* 2015; **63**: 1484-1490 [*RCA*] [PMID: 26297917 DOI: 10.1016/j.jhep.2015.08.011] [FullText]

90 **Singh P**, Garg PK. Pathophysiological mechanisms in acute pancreatitis: Current understanding. *Indian J Gastroenterol* 2016; **35**: 153-166 [*RCA*] [PMID: 27206712 DOI: 10.1007/s12664-016-0647-y] [FullText]

91 **Whitcomb DC**, Buchner AM, Forsmark CE. AGA Clinical Practice Update on the Epidemiology, Evaluation, and Management of Exocrine Pancreatic Insufficiency: Expert Review. *Gastroenterology* 2023; **165**: 1292-1301 [*RCA*] [PMID: 37737818 DOI: 10.1053/j.gastro.2023.07.007] [FullText]

92 **Singal AK**, Wong RJ, Dasarathy S, Abdelmalek MF, Neuschwander-Tetri BA, Limketkai BN, Petrey J, McClain CJ. ACG Clinical Guideline: Malnutrition and Nutritional Recommendations in Liver Disease. *Am J Gastroenterol* 2025; **120**: 950-972 [*RCA*] [PMID: 40314389 DOI: 10.14309/ajg.0000000000003379] [FullText] [Full Text(PDF)]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2025 Baishideng Publishing Group Inc. All rights reserved.